Abstract: P1025

Title: A PILOT STUDY OF THE ANTI-SLAMF7 MONOCLONAL ANTIBODY, ELOTUZUMAB, IN PATIENTS WITH MYELOFIBROSIS.

Abstract Type: Poster Presentation

Session Title: Myeloproliferative neoplasms - Clinical

Background:

Thrombopoietin receptor (MPL) activation induces fibrocyte differentiation and blood monocytes highly expressing MPL and signaling lymphocyte activation molecule family member 7 (SLAMF7) are possible fibrocyte precursors (Maekawa, *Leukemia* 2018). Elotuzumab (Elo), a SLAMF7-targeting monoclonal antibody, inhibited the differentiation of MF patient-derived fibrocytes *in vitro* and romiplostim-induced bone marrow (BM) fibrosis and splenomegaly *in vivo* (Maekawa, *Blood* 2019).

Aims:

To explore the efficacy and safety of Elo in patients with myelofibrosis (MF).

Methods:

This is a single-institution, investigator-initiated, pilot phase 2 study (NCT04517851) of Elo in patients (pts) with primary or post-polycythemia vera/essential thrombocythemia MF who are not candidates for JAK inhibitor (JAKi) therapy (prior JAKi permitted). Elo is dosed intravenously weekly at 10 mg/kg/w for the first 8 w, followed by 20 mg/kg q4w, and continued until disease progression or unacceptable toxicity (max 36 cycles). Spleen and liver sizes are measured by palpation and the MPN-SAF-TSS questionnaire (Emanuel, *J Clin Oncol* 2012) is administered on day 1 of each cycle. Pts receive a BM biopsy at screening and every 6 cycles on-study. Plasma cytokines are measured at baseline and every 3 cycles on-study. Responses are adjudicated by the revised IWG-MRT-ELN criteria (Tefferi, *Blood* 2013) and must last ≥12 w. In pts with baseline (BL) plts $<100 \times 10^9$/L, major, intermediate and minor plt responses are defined as ≥75%, 50-74% and 25-49% increases from BL. Elo is provided by Bristol-Myers Squibb. Extensive correlative studies are in progress.

Results:

Eleven pts had been treated as of the data cutoff date (Feb 14, 2023). BL characteristics appear in the **Table.** One pt had returned to chronic phase primary MF at study entry after successful treatment for transformation to acute myeloid leukemia (AML). Six pts continue on-study; reasons for discontinuation include lack of response in 3 pts, transformation to AML in 1 pt, and death from unrelated medical complications in 1 pt. Ten pts have completed the initial weekly dosing phase.

Two pts experienced clinical improvement (CI) in symptoms (sx) lasting 11.9 and 7.4 m, respectively; the first pt (now deceased from a GI bleed) also had a major plt response that lasted 15.3 m. This pt also experienced a decrease in erythrocyte transfusion frequency, but not transfusion independence (TI). Times to response for the 2 CI-sx responses were 3.7 and 0.9 m, respectively. Time to the plt response was 0.3 m. An additional pt had a TI response lasting 12 w, but subsequently lost it.

Two other pts have had ≥2 g/dL improvements in Hgb; one subsequently came off-study and one remains on-study. One pt had improvement in BM fibrosis grade from MF-3 to MF-2 after 2.8 m and continues on-study. One pt experienced disease progression to AML and was taken off-study.

Elo was very well-tolerated. One pt each experienced grade 1 headache, grade 1 hyperglycemia, grade 2 infusion reaction (chills) and grade 3 diarrhea felt to be possibly related to elo. There were 3 deaths on-study, all unrelated to elo: one from GI hemorrhage, one due to pneumonia/multi-organ failure and one from infection at an outside hospital (details unknown).

Updated clinical results, as well as results from correlative studies, will be presented.

Summary/Conclusion: Elo is active in the treatment of MF and has an excellent safety profile. A total of 15 pts are planned to be accrued to this pilot study. Future studies in combination with JAKi therapy appear warranted.

Table: Baseline characteristics of the patients

Characteristics		n=11
Median age (range)		71 (42 - 91) years
Diagnosis	PMF	9
	PET-MF	2
Gender	Male	5
Median bsln Hgb (range)		8.9 (6.4 - 13.5) g/dL
Median bsln WBC (range)		3.9 (1.8 - 15.7)
Median bsln PLT (range)		100 (8 - 563)
Karyotype	Abnormal	3
Driver mutation	*JAK2*	7
	CALR	0 (not done in 1)
	MPL	2 (not done in 1)
	Triple Negative	1
DIPSS-Plus Category	Low	1
	Int-1	2
	Int-2	4
	High	4
Bone marrow fibrosis grade	MF-1	1
	MF-2	5
	MF-3	5
BM Blast	≥ 5	0
	< 5	10
	Not available	1
Splenomegaly	Yes	4

Keywords: Idiopathic myelofibrosis, Targeted therapy, Myelofibrosis, Myeloproliferative disorder